

Access DB#

SEARCH REQUEST FORM

Scientific and Technical Information Center

85646

Requester's Full Name: Zohreh Fay (STIC) Examiner #: 66646 Date: 1/29/03
 Art Unit: 1614 Phone Number 308-4604 Serial Number: 19973838 B
 Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEI

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: 8-ISO prostaglandins for glaucoma TherapyInventors (please provide full names): Steven Pados, Thomas Mittag, Bernard BeckerEarliest Priority Filing Date: 5/9/97

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

2) please search the claimed compounds
for the claimed use.

Thank,
Z. Fay

Rush Send Answer

TTC

SPC, AUG 15

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

STAFF USE ONLY

Type of Search

Vendors and cost where applicable

Searcher: <u>W</u>	NA Sequence (#) _____	STN <u>✓</u>
Searcher Phone #: <u>4604</u>	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <u>✓</u>	Questel/Orbit _____
Date Searcher Picked Up: <u>1/30/03</u>	Bibliographic _____	Dr.Link _____
Date Completed: <u>1/30/03</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: <u>15</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>500</u>	Other _____	Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 17:58:41 ON 30 JAN 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JAN 2003 HIGHEST RN 483275-57-6

DICTIONARY FILE UPDATES: 29 JAN 2003 HIGHEST RN 483275-57-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

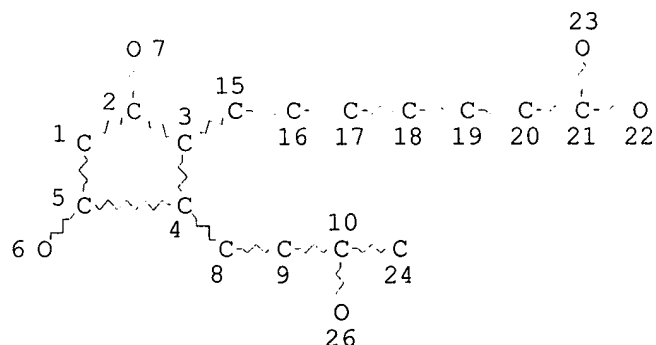
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que l33

L1 STR



NODE ATTRIBUTES:

CONNECT IS M1 RC AT 22

CONNECT IS M1 RC AT 24

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

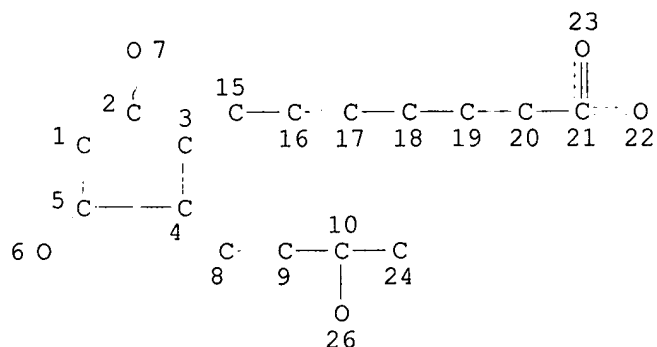
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L3 4523 SEA FILE=REGISTRY CSS FUL L1

L4 STR

Pat Delaval
Technical Librarian
Library & Chemical Library
606 277-7000/4400
patdelaval@cas.org



NODE ATTRIBUTES:

CONNECT IS M1 RC AT 22

CONNECT IS M1 RC AT 24

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

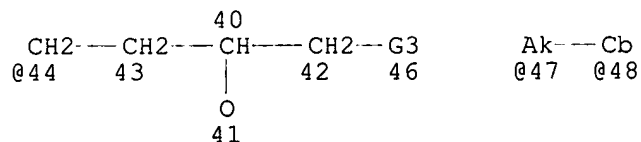
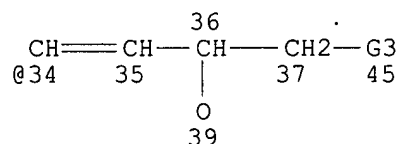
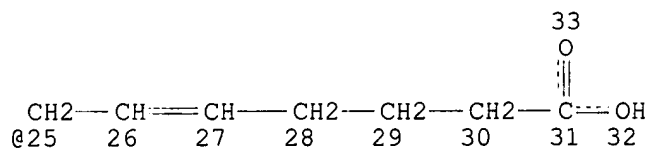
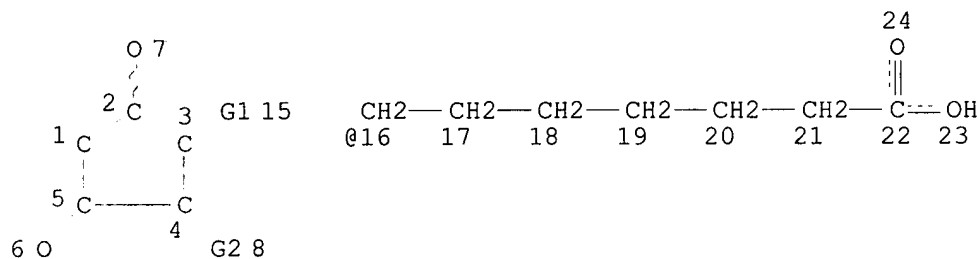
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L5 3628 SEA FILE=REGISTRY SUB=L3 SSS FUL L4

L31 STR



VAR G1=16/25

VAR G2=44/34

VAR G3=AK/CB/47/48

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 41

STEREO ATTRIBUTES: NONE

L32 667 SEA FILE=REGISTRY SUB=L5 CSS FUL L31

L33 7 SEA FILE=REGISTRY ABB=ON PLU=ON L32 AND 8 ISO?

=> d ide can tot l33

L33 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 31660-17-0 REGISTRY

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)-(.+-.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]-,
stereoisomer (8CI)

OTHER NAMES:

CN (.+-.)-8-Iso-PGE2

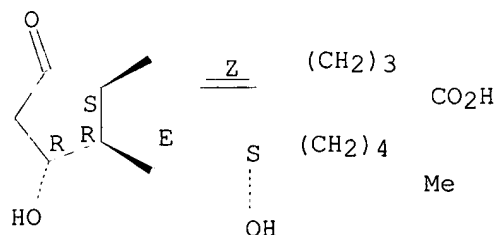
FS STEREOSEARCH

MF C20 H32 O5

LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1962 TO DATE)

11 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 89:197010

REFERENCE 2: 86:120875

REFERENCE 3: 86:106037

REFERENCE 4: 86:72018

REFERENCE 5: 86:43275

REFERENCE 6: 86:43274

REFERENCE 7: 86:43273

REFERENCE 8: 86:43272

REFERENCE 9: 86:43271

REFERENCE 10: 86:29419

L33 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 27415-26-5 REGISTRY

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
(5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-
(8CI)

OTHER NAMES:

CN 15-F2t-Isoprostane

CN 8-epi-PGF2.alpha.

CN 8-epi-Prostaglandin F2.alpha.

CN **8-Iso-PGF2.alpha.**

CN **8-iso-Prostaglandin F2.alpha.**

CN **8-Isoprostaglandin F2.alpha.**

CN Isoprostaglandin F2.alpha. type-III

FS STEREOSEARCH

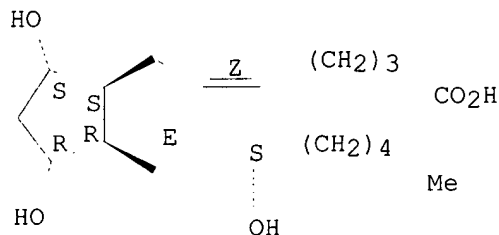
MF C20 H34 O5

LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT,
CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, MEDLINE,
TOXCENTER, USPATFULL

(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

352 REFERENCES IN FILE CA (1962 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

355 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37184

REFERENCE 2: 138:24095

REFERENCE 3: 138:19860

REFERENCE 4: 138:13506

REFERENCE 5: 137:367829

REFERENCE 6: 137:350753

REFERENCE 7: 137:346763

REFERENCE 8: 137:345874

REFERENCE 9: 137:310717

REFERENCE 10: 137:273303

L33 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 27415-25-4 REGISTRY

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]-,
stereoisomer (8CI)

OTHER NAMES:

CN **8-Iso-PGE2**

CN **8-Isoprostaglandin E2**

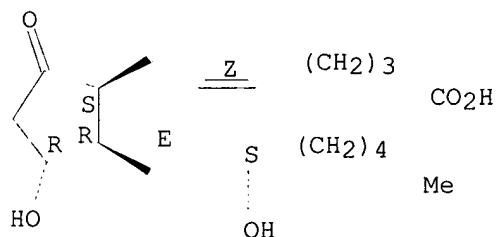
FS STEREOSEARCH

MF C20 H32 O5

LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS,
CHEMCATS, CSCHEM, EMBASE, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

66 REFERENCES IN FILE CA (1962 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

66 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:150553

REFERENCE 2: 137:77200

REFERENCE 3: 137:16027

REFERENCE 4: 136:32048

REFERENCE 5: 135:236932

REFERENCE 6: 135:147536

REFERENCE 7: 135:29381

REFERENCE 8: 134:361713

REFERENCE 9: 134:188516

REFERENCE 10: 134:126406

L33 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 26771-96-0 REGISTRY

CN Prost-13-en-1-oic acid, 9,11,15-trihydroxy-, (8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3,5-dihydroxy-2-(3-hydroxy-1-octenyl)-,
stereoisomer (8CI)

OTHER NAMES:

CN 8-Epi-PGF1.alpha.

CN **8-Isoprostaglandin F1.alpha.**

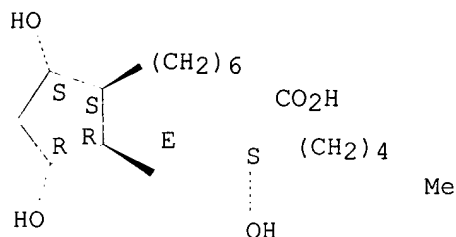
FS STEREOSEARCH

MF C20 H36 O5

LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, CSCHEM, IFICDB, IFIPAT,
IFIUDB, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18 REFERENCES IN FILE CA (1962 TO DATE)

18 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:247522

REFERENCE 2: 137:150553

REFERENCE 3: 135:29381

REFERENCE 4: 134:880

REFERENCE 5: 132:232274

REFERENCE 6: 127:76160

REFERENCE 7: 99:206351

REFERENCE 8: 98:628

REFERENCE 9: 96:15330

REFERENCE 10: 90:201042

L33 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 26771-95-9 REGISTRY

CN Prost-13-en-1-oic acid, 9,11,15-trihydroxy-, (8.beta.,9.beta.,11.alpha.,13
E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3,5-dihydroxy-2-(3-hydroxy-1-octenyl)-,
stereoisomer (8CI)

OTHER NAMES:

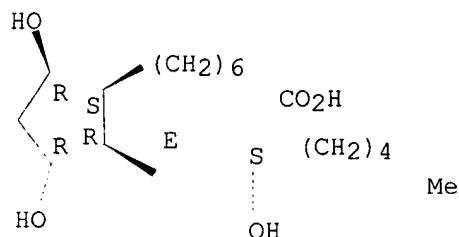
CN **8-Isoprostaglandin F1.beta.**

FS STEREOSEARCH

MF C20 H36 O5

LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, IFICDB, IFIPAT, IFIUDB,
USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1962 TO DATE)
10 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:247522
REFERENCE 2: 135:29381
REFERENCE 3: 134:880
REFERENCE 4: 127:76160
REFERENCE 5: 73:109365
REFERENCE 6: 73:3535
REFERENCE 7: 72:132154
REFERENCE 8: 72:109830
REFERENCE 9: 72:100143
REFERENCE 10: 72:100140

L33 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 21003-46-3 REGISTRY

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-,
(8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxo-,
stereoisomer (8CI)

OTHER NAMES:

CN 11.alpha.,15-(S)-Dihydroxy-9-oxo-13-trans-8-isoprostenoic acid

CN 8-Iso-PGE1

CN 8-iso-PGE1

CN 8-Isoprostaglandin E1

CN Isoprostaglandin E1

CN Ovinonic acid

FS STEREOSEARCH

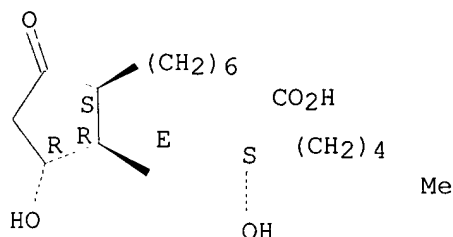
DR 23756-23-2

MF C20 H34 O5

LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM,
EMBASE, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL

(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

40 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
40 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:150553
REFERENCE 2: 135:29381
REFERENCE 3: 134:188516
REFERENCE 4: 134:880
REFERENCE 5: 132:232274
REFERENCE 6: 131:238301
REFERENCE 7: 130:13467
REFERENCE 8: 130:10658
REFERENCE 9: 129:131581
REFERENCE 10: 128:304157

L33 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 7045-31-0 REGISTRY

CN Prosta-5,13,17-trien-1-oic acid, 9,11,15-trihydroxy-,
(5Z,8.beta.,9.alpha.,11.alpha.,13E,15S,17Z)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3.alpha.,5.alpha.-dihydroxy-2-(3-hydroxy-1,5-octadienyl)cyclopentyl]- (7CI, 8CI)

OTHER NAMES:

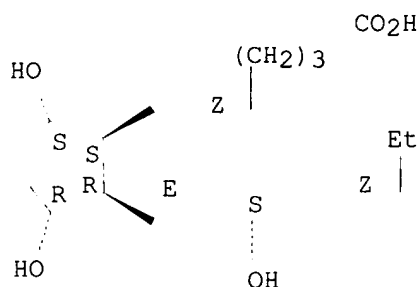
CN **8-Iso-PGF3.alpha.**

FS STEREOSEARCH

MF C20 H32 O5

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1962 TO DATE)
 13 REFERENCES IN FILE CAPLUS (1962 TO DATE)
 2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:335491
 REFERENCE 2: 135:29381
 REFERENCE 3: 134:361713
 REFERENCE 4: 134:126402
 REFERENCE 5: 134:880
 REFERENCE 6: 132:232274
 REFERENCE 7: 131:252650
 REFERENCE 8: 131:238301
 REFERENCE 9: 130:320932
 REFERENCE 10: 127:171810

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 17:59:02 ON 30 JAN 2003

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FILE COVERS 1907 - 30 Jan 2003 VOL 138 ISS 5

FILE LAST UPDATED: 29 Jan 2003 (20030129/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 161

L61 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 AN 1998:744935 HCAPLUS
 DN 130:10658
 TI **8-Isoprostaglandins for glaucoma therapy**
 IN **Podos, Steven M.; Mittag, Thomas W.; Becker, Bernard**
 PA The Mount Sinai School of Medicine of the City University of New York, USA
 SO PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-215
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850024	A1	19981112	WO 1998-US9090	19980506 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9873686	A1	19981127	AU 1998-73686	19980506 <--
	AU 725677	B2	20001019		
	US 6037368	A	20000314	US 1998-73552	19980506 <--
	EP 1007028	A1	20000614	EP 1998-920974	19980506 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1997-853803	A2	19970509 <--		
	WO 1998-US9090	W	19980506		
OS	MARPAT 130:10658				
AB	The invention relates to the use of 8-isoprostaglandins and their derivs. for decreasing intraocular pressure, e.g. in the treatment of glaucoma . It is based, at least in part, on the discovery that 8-isoprostaglandin E2 effectively decreased intraocular pressure by a trabecular meshwork outflow mechanism.				
ST	isoprostaglandin glaucoma treatment				
IT	Drug delivery systems				
	Glaucoma (disease)				
	(isoprostaglandins for glaucoma therapy)				
IT	Prostaglandins				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(isoprostaglandins for glaucoma therapy)				
IT	21003-46-3 21003-46-3D, derivs. 27415-25-4				
	27415-25-4D, derivs. 27415-26-5 27415-26-5D, derivs.				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(isoprostaglandins for glaucoma therapy)				

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bito; US 4599353 A 1986 HCAPLUS

IT 21003-46-3 21003-46-3D, derivs. 27415-25-4
 27415-25-4D, derivs. 27415-26-5 27415-26-5D, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

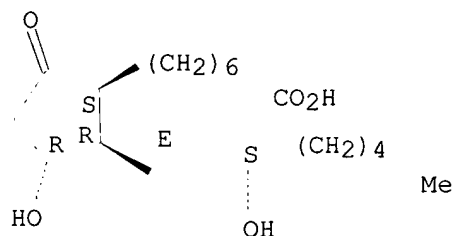
(isoprostaglandins for **glaucoma** therapy)

RN 21003-46-3 HCAPLUS

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-,
(8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

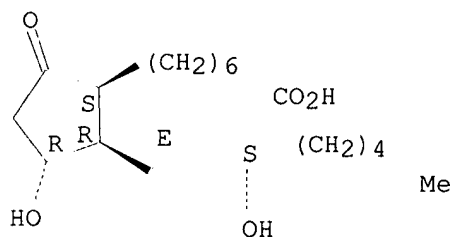


RN 21003-46-3 HCAPLUS

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-,
(8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

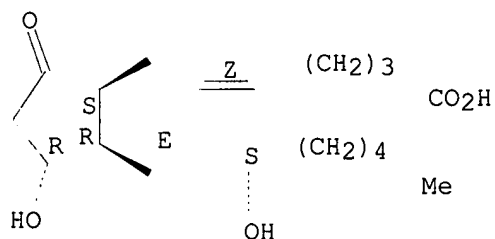


RN 27415-25-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

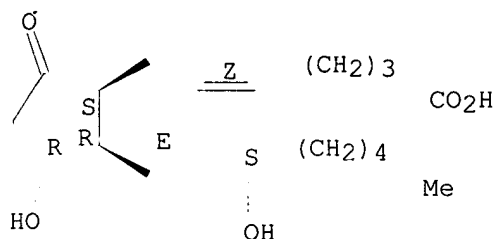


RN 27415-25-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

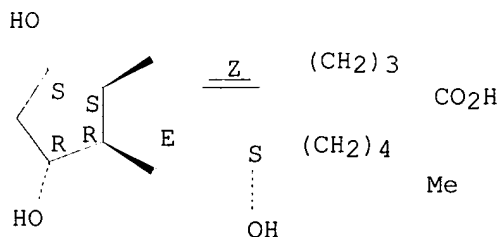
Absolute stereochemistry.

Double bond geometry as shown.



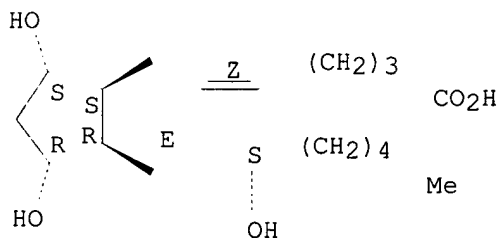
RN 27415-26-5 HCAPLUS
 CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
 (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



RN 27415-26-5 HCAPLUS
 CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
 (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



L61 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 AN 1994:465605 HCAPLUS
 DN 121:65605
 TI Prostaglandins for the treatment of **glaucoma**
 IN Woodward, David F.
 PA Allergan, Inc., USA
 SO PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-557
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1

FAN.CNT 1

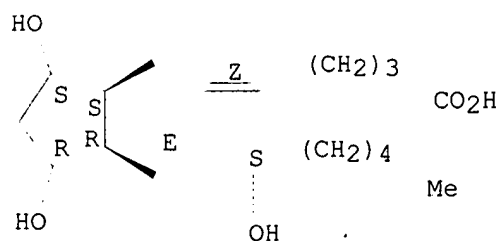
PATENT NO.

KIND DATE

APPLICATION NO. DATE

PI WO 9411002 A1 19940526 WO 1993-US10853 19931109 <--
 W: AU, CA, HU, JP, NZ
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 US 6124353 A 20000926 US 1992-975194 19921112 <--
 AU 9455986 A1 19940608 AU 1994-55986 19931109 <--
 PRAI US 1992-975194 A 19921112 <--
 WO 1993-US10853 W 19931109 <--
 OS MARPAT 121:65605
 AB **Glaucoma** is treated by applying to the eye an amt. sufficient to
 treat **ocular hypertension** of prostaglandins of the D,
 E, and F series, or a pharmaceutically acceptable salt thereof.
 Intraocular pressure-reducing activities of 8-epi PGF2.alpha. and 8-epi
 PGF2.alpha. 1-Me ester were demonstrated with rabbits and monkeys.
 ST ophthalmic prepn prostaglandin **glaucoma**
 IT **Glaucoma (disease)**
 (treatment of, with ophthalmic prepn. contg. prostaglandins)
 IT Prostaglandins
 RL: BIOL (Biological study)
 (D, ophthalmic prepn. contg., for treatment of **ocular**
hypertension)
 IT Prostaglandins
 RL: BIOL (Biological study)
 (E, ophthalmic prepn. contg., for treatment of **ocular**
hypertension)
 IT Prostaglandins
 RL: BIOL (Biological study)
 (F, ophthalmic prepn. contg., for treatment of **ocular**
hypertension)
 IT Pharmaceutical dosage forms
 (ophthalmic, prostaglandins in, for treatment of **ocular**
hypertension)
 IT 27415-26-5 96244-10-9
 RL: BIOL (Biological study)
 (ophthalmic prepn. contg., for treatment of **ocular**
hypertension)
 IT 27415-26-5
 RL: BIOL (Biological study)
 (ophthalmic prepn. contg., for treatment of **ocular**
hypertension)
 RN 27415-26-5 HCAPLUS
 CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
 (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



=> fil uspatall

FILE 'USPATFULL' ENTERED AT 18:13:09 ON 30 JAN 2003

CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 18:13:09 ON 30 JAN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib ab kwic hitstr tot 186

L86 ANSWER 1 OF 2 USPATFULL
AN 2000:128385 USPATFULL
TI Method of treating **ocular hypertension** with 8-epi
prostaglandins
IN Woodward, David F., El Toro, CA, United States
PA Allergan Sales, Inc., Irvine, CA, United States (U.S. corporation)
PI US 6124353 20000926
AI US 1992-975194 19921112 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Cintins, Marianne
LREP Baran, Robert J., Voet, Martin A., Fisher, Carlos A.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 554

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method of treating **ocular hypertension** which comprises applying to the eye an amount sufficient to treat **ocular hypertension** of a compound of formula (I) ##STR1## wherein the wavy line attachments indicate either alpha (.alpha.) or beta (.beta.) configuration; hatched lines indicate .alpha. configuration, solid triangles are used to indicate .beta. configuration; the dashed bonds represent a single bond or a double bond which can be in the cis or trans configuration; X is selected from the group consisting of H, R or a pharmaceutically-acceptable cation, and R is an aliphatic hydrocarbon group of about 1 to about 6 carbon atoms; one of R.sub.1 and R.sub.2 is .dbd.O, --OH or an --O(CO)R.sub.4 group, and the other one is --OH or an --O(CO)R.sub.4 group or R.sub.1 is .dbd.O and R.sub.2 is H; R.sub.3 is --OH or --O(CO)R.sub.4, wherein R.sub.4 is a saturated or unsaturated acyclic hydrocarbon group having from 1 to about 20 carbon atoms, or --(CH.sub.2).sub.n R.sub.5 wherein n is 0-10, and R.sub.5 is an aliphatic ring from about 3 to about 7 carbon atoms, or an aromatic or heteroaromatic ring; or a pharmaceutically acceptable salt thereof.

TI Method of treating **ocular hypertension** with 8-epi
prostaglandins

AB The present invention provides a method of treating **ocular hypertension** which comprises applying to the eye an amount sufficient to treat **ocular hypertension** of a compound of formula (I) ##STR1## wherein the wavy line attachments indicate either alpha (.alpha.) or beta (.beta.) configuration;. . .
SUMM . . . prostaglandins and C-1 ester derivatives thereof. Such compounds are potent ocular hypotensives, and are particularly suitable for the management of **glaucoma**.

SUMM . . . useful in the treatment of a number of ocular hypertensive conditions, such as post-surgical and post-laser trabeculectomy ocular hypertensive episodes, **glaucoma**, and as presurgical adjuncts.

SUMM **Glaucoma** is a disease of the eye characterized by increased intraocular pressure. On the basis of its etiology, **glaucoma** has been classified as primary or secondary. For example, primary **glaucoma** in adults (congenital **glaucoma**) may be either open-angle or acute or chronic angle-closure. Secondary **glaucoma** results from pre-existing ocular diseases such as uveitis, intraocular tumor or an enlarged cataract.

SUMM The underlying causes of primary **glaucoma** are not yet known. The increased intraocular tension is due to the obstruction of aqueous

humor outflow. In chronic open-angle **glaucoma**, the anterior chamber and its anatomic structures appear normal, but drainage of the aqueous humor is impeded. In acute or chronic angle-closure **glaucoma**, the anterior chamber is shallow, the filtration angle is narrowed, and the iris may obstruct the trabecular meshwork at the. . . produce pupillary block and thus precipitate an acute attack. Eyes with narrow anterior chamber angles are predisposed to acute angle-closure **glaucoma** attacks of various degrees of severity.

SUMM Secondary **glaucoma** is caused by any interference with the flow of aqueous humor from the posterior chamber into the anterior chamber and. . .

SUMM Considering all types together, **glaucoma** occurs in about 2% of all persons over the age of 40 and may be asymptotic for years before progressing. . . vision. In cases where surgery is not indicated, topical .beta.-adrenoreceptor antagonists have traditionally been the drugs of choice for treating **glaucoma**.

SUMM . . . shows that some prostaglandins are highly effective ocular hypotensive agents, and are ideally suited for the long-term medical management of **glaucoma** (see, for example, Bito, L. Z. Biological Protection with Prostaglandins Cohen, M. M., ed., Boca Raton, Fla., CRC Press Inc., 1985, pp. 231-252; and Bito, L. Z., Applied Pharmacology in the Medical Treatment of **Glaucomas** Drance, S. M. and Neufeld, A. H. eds., New York, Grune & Stratton, 1984, pp. 477-505). Such prostaglandins include PGF.sub.2.alpha.,. . .

SUMM . . . C.sub.5 alkyl esters of the latter compound, were reported to possess ocular hypotensive activity and were recommended for use in **glaucoma** management. It was suggested that the C.sub.1 to C.sub.5 alkyl esters of PGF.sub.2.alpha., such as its methyl and isopropyl esters,. . .

SUMM . . . 1-isopropyl ester, in humans. The clinical potentials of prostaglandins in the management of conditions associated with increased ocular pressure, e.g. **glaucoma** are greatly limited by these side effects.

SUMM In one aspect, the present invention relates to a method of treating **ocular hypertension** which comprises applying to the eye an amount sufficient to treat **ocular hypertension** of a compound of formula (I) ##STR2## wherein the wavy line attachments indicate either alpha (.alpha.) or beta (.beta.) configuration;. . .

SUMM In a preferred embodiment, such pharmaceutical compositions are in the form of ophthalmic solutions for the treatment of **ocular hypertension**, comprising an amount sufficient to treat **ocular hypertension** of a compound of formula (I) as hereinabove defined, or a pharmaceutically acceptable salt thereof.

CLM What is claimed is:

1. A method of treating **ocular hypertension** which comprises applying to the eye an amount sufficient to treat **ocular hypertension** of a compound of formula (I) while lowering hyperemia as compared to the corresponding iso form of the compound ##STR7##. . .
11. The pharmaceutical composition of claim 10 wherein said aqueous solution is an ophthalmic solution for the treatment of **ocular hypertension** comprising an amount sufficient to treat **ocular hypertension** of said compound of formula (I) or an ophthalmically acceptable salt thereof.

IT **Glaucoma (disease)**
(treatment of, with ophthalmic preps. contg. prostaglandins)

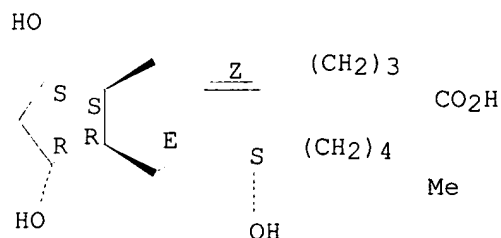
IT 27415-26-5 96244-10-9
(ophthalmic preps. contg., for treatment of ocular hypertension)

IT 27415-26-5
(ophthalmic preps. contg., for treatment of ocular hypertension)

RN 27415-26-5 USPATFULL

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
(5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L86 ANSWER 2 OF 2 USPATFULL

AN 2000:31442 USPATFULL

TI 8-iso- prostaglandins for **glaucoma** therapy

IN Podos, Steven M., Tenafly, NJ, United States

Mittag, Thomas W., Pleasantville, NY, United States

Becker, Bernard, University City, MO, United States

PA Mount Sinai School of Medicine, New York, NY, United States (U.S. corporation)

PI US 6037368 20000314

AI US 1998-73552 19980506 (9)

RLI Continuation of Ser. No. US 1997-853803, filed on 9 May 1997, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Fay, Zohreh

LREP Bakerbotts LLP

CLMN Number of Claims: 21

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 381

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the use of 8-iso prostaglandins and their derivatives for decreasing intraocular pressure, for example in the treatment of **glaucoma**. It is based, at least in part, on the discovery that 8-iso prostaglandin E.sub.2 effectively decreased intraocular pressure by a trabecular meshwork outflow mechanism.

TI 8-iso- prostaglandins for **glaucoma** therapy

AB . . . relates to the use of 8-iso prostaglandins and their derivatives for decreasing intraocular pressure, for example in the treatment of **glaucoma**. It is based, at least in part, on the discovery that 8-iso prostaglandin E.sub.2 effectively decreased intraocular pressure by a . . .

SUMM . . . relates to the use of 8-iso prostaglandins and their derivatives for decreasing intraocular pressure, for example in the treatment of **glaucoma**. It is based, at least in part, on the discovery that 8-iso prostaglandin E.sub.2 effectively decreased intraocular pressure by a . . .

SUMM **Glaucoma** is a major eye disease which can cause progressive loss of vision leading to blindness. The majority of human **glaucomas** are associated with increased intraocular pressure ("IOP") resulting from an imbalance in the rate of secretion of aqueous humor by . . . humor outflow from these chambers, primarily via the canal of Schlemm. High IOP is considered the major risk factor for **glaucomatous** visual impairment resulting from the death of retinal ganglion cells, loss of the nerve fiber layer in the retina, and. . .

SUMM **Glaucoma** is typically classified, on the basis of its

etiology, as primary or secondary. Primary **glaucoma** in adults, a disorder in which the underlying cause is poorly understood, is associated with increased IOP due to an. . . open angle or acute or chronic angle closure. The anterior chamber of the eye appears normal in chronic open angle **glaucoma**, despite impaired drainage of aqueous humor. In contrast, the anterior chamber is shallow and the filtration angle is narrowed in chronic angle-closure **glaucoma**, wherein the trabecular meshwork and the canal of Schlemm may be obstructed by the iris. An acute attack of **glaucoma** may arise in this context when the pupil dilates, pushing the root of the iris forward to block the angle.

SUMM Secondary **glaucoma** is caused by another disorder which functionally interferes with the outflow of aqueous humor or the flow from the posterior. . . .

SUMM . . . decreasing the formation of aqueous humor within the eye. Pilocarpine and epinephrine are clinical agents that also lower IOP in **glaucomatous** eyes, but these drugs act principally by decreasing the resistance in the trabecular meshwork outflow channels. A third mechanism for. . . prostaglandin derivative belonging to the F2.alpha. series of prostanoids, which acts primarily by this uveoscleral mechanism, has been introduced for **glaucoma** therapy. This drug, called latanoprost, is the isopropyl ester of a compound having the following structure: ##STR1##

SUMM Prostaglandins which may be used in the treatment of **glaucoma** are described in U.S. Pat. Nos. 5,476,872 by Garst et al., 4,599,353 by Bito, 5,262,437 by Chan, 5,462,968 by Woodward,. . . .

SUMM The present invention relates to prostaglandins which are structurally different from latanoprost and other prostaglandins used in the treatment of **glaucoma**, and that belong to the 8-iso series of prostanoids, for example 8-iso PGE.sub.2, 8-iso PGE.sub.2 and 8-iso-PGF.sub.2.alpha.. In contrast to. . . .

SUMM . . . use of 8-iso prostanoids in methods which decrease intraocular pressure ("IOP") in the eye, for example in the treatment of **glaucoma**. The 8-iso-prostanoids of the invention have a common structure according to formula I: ##STR2## where either bond W or bond.

SUMM . . . advantage in that the trabecular meshwork is the primary locus of the pathology causing increased IOP in primary open angle **glaucoma**.

SUMM . . . the invention to a subject in need of such treatment. Such a method may be used in the treatment of **glaucoma** in a subject. Suitable formulations include for example, and not by way of limitation, a topical solution which is a. . . .

SUMM According to the invention, IOP may be decreased, and/or **glaucoma** may be treated, using compositions comprising an 8-iso prostanoid of the invention as the sole active agent, or in conjunction.

DETD Experiments were performed to evaluate the effects of single dose administration of 8-iso PGE.sub.2 on IOP in normal ("N") and **glaucomatous** ("G") monkey eyes, and to determine the mechanism by which 8-iso PGE.sub.2 alters IOP in N monkey eyes, when applied. .

DETD Table 2 shows the effect of 8-iso PGE.sub.2 on IOP and outflow facility in **glaucomatous** monkey eyes. Because of the individual variability in laser-induced **glaucomatous** monkey eyes, the IOP and facility measurements are expressed in the table as ratios (value of the drug-treated eye.div.the value of the vehicle-treated eye). The ratios were calculated from the values of the same **glaucomatous** monkey eye determined immediately prior to administration of the drug or the vehicle (time 0 hrs.), and the values at. . . of the drug or vehicle. The data in Table 2 show that in the primate, administration of 8-iso PGE.sub.2 to **glaucomatous** eyes significantly lowers IOP (by 13.8%) and significantly increases outflow facility (by 38.8%),

which is of sufficient magnitude to account for the fall in IOP. Thus the mechanism of lowering IOP by 8-iso PGE.sub.2 in both normal and **glaucomatous** eyes is primarily due to an increase in aqueous humor trabecular outflow.

DETD

TABLE 2

Effect of 0.1% 8-iso PGE.sub.2 on IOP and Outflow Facility Responses in 8 **Glaucomatous** Monkey Eyes (Unilateral)

Time	Intraocular Pressure		Outflow facility	
	(drug-treated/ vehicle-treated)	(drug-treated/ vehicle-treated)	(drug-treated/ vehicle-treated)	(drug-treated/ vehicle-treated)
0 hr				
2 hr				

Response.

DETD . . . single dose of 8-iso PGE, (the 13, 14 dihydro derivative of 8-iso PGE.sub.2), 8-iso PGE.sub.2, or 8-iso PGF.sub.2.alpha. in laser-induced **glaucomatous** eyes in cynomolgus monkeys (wherein only one eye is rendered **glaucomatous** and the other serves as a control). Following one day of baseline IOP measurement, a single 25 .mu.l dose of. . . percent 8-iso PGE.sub.1, or (ii) 0.1 percent 8-iso PGE.sub.2, or (iii) 0.1 percent 8-iso PGF.sub.2.alpha., was topically applied to the **glaucomatous** eye in groups of 4 or 8 monkeys. It was found that 8-iso PGE.sub.1 (0.1 percent) reduced IOP (p<0.05) for up to four hours in **glaucomatous** monkey eyes (n=4). The maximum reduction in IOP was 5.3+-.0.8 (mean+-.SEM) mm Hg at 2 hours after dosing. 8-iso PGE.sub.2. . . the compounds tested, 8-iso PGE.sub.2 appears to have the greatest and 8-iso PGF.sub.2.alpha.. the least activity in decreasing IOP in **glaucomatous** monkey eyes.

IT Drug delivery systems

IT **Glaucoma (disease)**

(isoprostaglandins for glaucoma therapy)

IT 21003-46-3 21003-46-3D, derivs. 27415-25-4
27415-25-4D, derivs. 27415-26-5 27415-26-5D,
derivs.

(isoprostaglandins for glaucoma therapy)

IT 21003-46-3 21003-46-3D, derivs. 27415-25-4
27415-25-4D, derivs. 27415-26-5 27415-26-5D,
derivs.

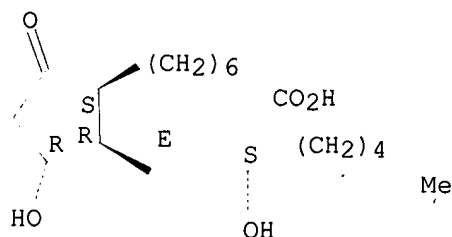
(isoprostaglandins for glaucoma therapy)

RN 21003-46-3 USPATFULL

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-,
(8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

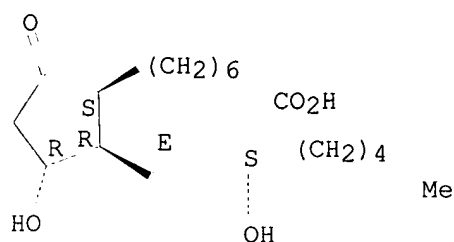
Double bond geometry as shown.



RN 21003-46-3 USPATFULL

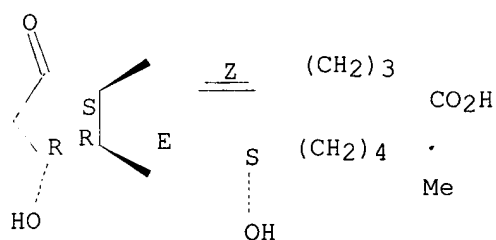
CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-,
(8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



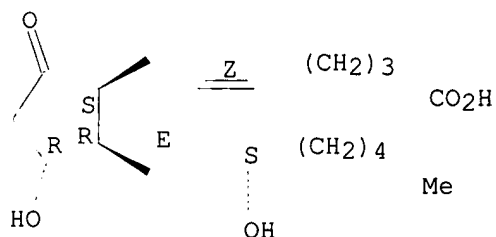
RN 27415-25-4 USPATFULL
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



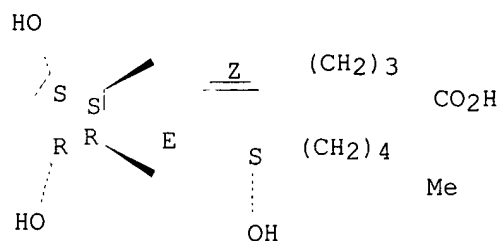
RN 27415-25-4 USPATFULL
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
(5Z,8.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



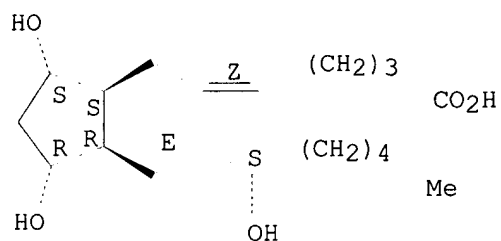
RN 27415-26-5 USPATFULL
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
(5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 27415-26-5 USPATFULL
 CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
 (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



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(FILE 'HOME' ENTERED AT 17:16:52 ON 30 JAN 2003)

FILE 'REGISTRY' ENTERED AT 17:17:14 ON 30 JAN 2003

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      SET COST OFF
L1      STR
L2      50 S L1 CSS
L3      4523 S L1 CSS FUL
      SAV TEMP L3 FAY073/A
L4      STR L1
L5      3628 S L4 FUL SUB=L3
      SAV TEMP L5 FAY073A/A
L6      STR L4
L7      0 S L6 FUL SUB=L5
L8      STR L6
L9      50 S L8 SAM SUB=L5
L10     1817 S L8 FUL SUB=L5
      SAV L10 TEMP FAY073B/A
L11     STR L8
L12     829 S L11 FUL SUB=L10
      SAV TEMP L12 FAY073C/A
L13     STR L11
L14     12 S L13 CSS SAM SUB=L12
L15     338 S L13 CSS FUL SUB=L12
      SAV L15 TEMP FAY073D/A

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FILE 'HCAPLUS' ENTERED AT 17:36:00 ON 30 JAN 2003

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      E PODOS S/AU
L16     100 S E5,E6,E8
      E MITTAG T/AU

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L17 92 S E3,E4,E6-E12
 E BECKER B/AU
 L18 385 S E3-E18,E40-E43
 L19 14388 S L15
 L20 8 S L16-L18 AND L19
 SEL RN

FILE 'REGISTRY' ENTERED AT 17:38:10 ON 30 JAN 2003

L21 13 S E1-E13
 L22 2 S L21 AND L15
 L23 4 S L21 AND L3
 L24 4 S L22,L23
 L25 9 S L21 NOT L24
 L26 2 S L23 NOT L22
 L27 4 S L5 AND L21
 L28 2 S L10 AND L21
 L29 STR L8
 L30 50 S L29 SAM SUB=L5
 L31 STR L13
 L32 667 S L31 CSS FUL SUB=L5
 SAV L32 FAY073E/A
 L33 7 S L32 AND 8 ISO?

FILE 'HCAOLD' ENTERED AT 17:47:04 ON 30 JAN 2003

L34 2 S L33
 SEL AN
 EDIT /AN /OREF

FILE 'HCAPLUS' ENTERED AT 17:47:25 ON 30 JAN 2003

L35 3 S E14-E15

FILE 'HCAOLD' ENTERED AT 17:49:03 ON 30 JAN 2003

FILE 'HCAOLD' ENTERED AT 17:49:07 ON 30 JAN 2003

FILE 'HCAPLUS' ENTERED AT 17:49:13 ON 30 JAN 2003

L36 424 S L33
 L37 7 S L36 AND L16-L18
 L38 157 S L36 AND (PD<=19970509 OR PRD<=19970509 OR AD<=19970509)
 L39 2 S L38 AND ?GLAUCOM?
 E GLAUCOMA/CT
 L40 2997 S E3-E6,E12
 E E4+ALL
 L41 2936 S E5,E4
 E E10_ALL
 E GLAUCOMA/CT
 E E4+ALL
 L42 2936 S E4,E5
 L43 4580 S E6-E9/BI
 E E10+ALL
 L44 975 S E3
 L45 1159 S E3-E6/BI
 L46 2 S L38 AND L40-L45
 L47 35768 S L32
 L48 30307 S L47 AND (PD<=19970509 OR PRD<=19970509 OR AD<=19970509)
 L49 85 S L48 AND L40-L45
 L50 75 S L48 AND ?GLAUCOM?
 L51 86 S L49,L50
 L52 1 S L51 AND 8 ISO?
 E PROSTAGLANDIN/CT
 E E58+ALL
 L53 537 S E3 (L) ISO?
 L54 5 S L53 AND L40-L45

L55 5 S L53 AND ?GLAUCOM?
L56 5 S L54,L55
L57 6 S L39,L46,L52,L56
L58 2 S L57 AND 8 ISO?
L59 3 S L57,L58 AND (PD<=19970509 OR PRD<=19970509 OR AD<=19970509)
L60 2 S L59 NOT RABBITS/TI
L61 2 S L60 AND L16-L20,L35-L60

FILE 'REGISTRY' ENTERED AT 17:58:41 ON 30 JAN 2003

FILE 'HCAPLUS' ENTERED AT 17:59:02 ON 30 JAN 2003

FILE 'MEDLINE' ENTERED AT 18:00:02 ON 30 JAN 2003

L62 125 S L33
L63 3 S L62 AND ?GLAUCOM?
L64 3 S L62 AND L43,L45
L65 3 S L63,L64
E PROSTAGLANDIN/CT
E PROSTAGLANDINS/CT
E E3+ALL
L66 69795 S E51+NT
L67 59887 S L66,L62 AND PY<=1997
L68 196 S L67 AND L43,L45
E GLAUCOMA/CT
E E3+ALL
L69 23660 S E4+NT
E E3+ALL
L70 24576 S E3+NT
L71 196 S L67 AND L43,L45
L72 162 S L67 AND L69,L70
L73 196 S L71,L72
L74 0 S L73 AND 8 ISO?
L75 3 S L65 AND L66
E PROSTAGLANDINS F/CT
E E4+ALL
L76 1270 S E52
L77 65 S L76 AND L73
E PROSTAGLANDINS E/CT
E E3=ALL
E PROSTAGLANDINS E/CT
E E3+ALL
L78 14072 S E50
E PROSTAGLANDINS E/CT
E E4+ALL
L79 1477 S E52
L80 18 S L73 AND L78,L79
L81 0 S L80 AND 8

FILE 'USPATFULL, USPAT2' ENTERED AT 18:12:21 ON 30 JAN 2003

L82 21 S L33
L83 2 S L82 AND ?GLAUCOM?
L84 2 S L82 AND L43,L45
E GLAUCOMA/CT
L85 2 S L82 AND E4
L86 2 S L83-L85

FILE 'USPATFULL, USPAT2' ENTERED AT 18:13:09 ON 30 JAN 2003